

IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (currently amended) A method for preparation of a modified host cell comprising:

- a) transfecting a host cell with at least one polynucleotide to which a label is covalently coupled; and
- b) isolating the transfected host cell, wherein said at least one polynucleotide permanently changes a metabolic property of the transfected host cell as compared to the non-transfected host cell;

wherein the label provides to the host cell a non-inheritable trait.

2. (original) A method according to claim 1, wherein isolation of the transfected host cell is established by direct separation of the host cells containing said label from host cells not containing said label.

3. (previously presented) A method according to claim 1, wherein isolation of the transfected host cell is established by using means that can distinguish and separate said transfected host cell containing said label from non-transfected host cells.

4. (previously presented) A method according to claim 1, wherein the label is selected from the group consisting of a fluorescent label, a luminescent label, a chemoluminescent label, a magnetic label, an antigenic label, an enzymatic label, and a radioactive label.

5. (original) A method according to claim 3, wherein the label is a fluorescent label and the means for detection is a Fluorescent Activated Cell Sorter (FACS).

6. (currently amended) A method according to claim 1, wherein the transfected host cell of [[step]] b) is subsequently cultured under proliferating conditions.

7. (currently amended) A method according to claim 1, wherein the modified host cell is not isolated by selection with at least one polynucleotide ~~does not comprise~~ an antibiotic or other ~~selection~~-marker which is an inheritable trait.

8. (currently amended) A method according to claim 1, wherein RNA and protein ~~DNA~~ expression levels ~~and/or RNA expression levels and/or protein expression levels~~ are altered in the modified ~~transfected~~-host cell as compared to the non-modified ~~transfected~~-host cell.

9. (previously presented) A method according to claim 1, wherein the modified host cell is a prokaryotic cell, a eukaryotic cell, a mammalian cell or a plant cell.

10. (withdrawn) A method for preparation of a desired compound by a transfected host cell comprising:

- a) transfecting a host cell with at least one polynucleotide involved in production of said desired compound and which is covalently coupled to a label which provides to the host cell a non-inheritable trait,
- b) isolating the transfected host, wherein said at least one polynucleotide permanently changes production of said desired compound of the transfected host cell as compared to the non-transfected host cell,
- c) culturing the transfected host cell under proliferating conditions,
- d) culturing the transfected host cell in broth under conditions wherein the desired compound is produced, and
- e) isolating the desired compound from the culture broth.

11. (withdrawn) A method according to claim 10, wherein the polynucleotide is selected from the group consisting of DNA, RNA, short hairpin RNA, non-coding RNA, LNA, HNA, and PNA.

12. (withdrawn) A method according to claim 10, wherein the polynucleotide modifies the titer, stability, isolation and/or activity of said desired compound.

13. (withdrawn) A method according to claim 10, wherein the desired compound is a protein.

14. (withdrawn) A method according to claim 10, wherein the desired compound is an enzyme.

15. (withdrawn-currently amended) A method for preparation of a modified host cell comprising:

- a) transfecting a host cell with at least one DNA which is covalently coupled to a fluorescent label that provides to the host cell a non-inheritable trait,
- b) isolating the transfected host cell by detecting the fluorescent label and then separating fluorescent host cells which were transfected from non-fluorescent host cells which were not transfected,
- c) culturing the transfected host cell such that fluorescently-labeled polynucleotide integrates into the host cell's genome,
- d) multiplying the transfected host cell which has polynucleotide integrated in its genome such that the fluorescent label is diluted and lost in progeny of the transfected host cell, and
- e) isolating from non-labeled progeny of the transfected host cell a modified host cell having a changed metabolic property as compared to the host cell prior to transfection.

16. (withdrawn) A method for preparation of a desired metabolite by a modified host cell comprising:

- a) preparing a modified host cell according to claim 15 wherein said DNA is involved in production of the desired metabolite,

- b) culturing the modified host cell in broth under conditions wherein the desired metabolite is produced, and
- c) isolating the desired metabolite from the culture broth.

17. (withdrawn) A method according to claim 16, wherein the desired metabolite is a primary metabolite.

18. (withdrawn) A method according to claim 16, wherein the desired metabolite is an amino acid, a steroid or a nucleotide.

19. (withdrawn) A method according to claim 16, wherein the desired metabolite is a secondary metabolite.

20. (withdrawn) A method according to claim 19, wherein the desired secondary metabolite is an antibiotic, a vitamin, an anti-infective, a macrolide, a polyketide, a pheromone, an alkaloid or a drug.

21. (withdrawn) A method for preparation of a desired biomass by a modified host cell comprising:

- a) preparing a modified host cell according to claim 15 wherein said at least one DNA is involved in production of the desired biomass,
- b) culturing the modified host cell under conditions wherein the desired biomass is produced, and
- c) isolating the desired biomass from the culture.

Claim 22 (canceled)

23. (withdrawn) A method according to claim 21, wherein the desired biomass is a yeast cell.

24. (withdrawn) A method according to claim 21, wherein the desired biomass comprises a biocatalyst.

25. (withdrawn) A method according to claim 21, wherein the desired biomass comprises screenable cells for drug discovery.

Claim 26 (canceled)

27. (withdrawn) A method according to claim 15, wherein the at least one DNA does not comprise an antibiotic or other selection marker which is an inheritable trait.

28. (withdrawn-currently amended) A method according to claim 15, wherein RNA and protein expression levels ~~and protein expression levels~~ are altered in the modified host cell as compared to the non-modified host cell.

29. (new) A method for preparation of a modified host cell comprising:

- a) transfecting host cells with at least one DNA to which a fluorescent label is covalently coupled;
- b) separating transfected host cells, which contain the fluorescent label, from non-transfected host cells, which do not contain the fluorescent label, by detection of the fluorescent label; and
- c) isolating a modified host cell from the separated and transfected host cells, wherein the at least one DNA integrates into the modified host cell's genome thereby permanently changing a metabolic property of transfected host cells as compared to non-transfected host cells.

30. (new) A method according to claim 29, wherein the transfected host cells are cultured under proliferating conditions between their separation and isolation.

32. (new) A method according to claim 29, wherein the modified host cell is not isolated by selection with an antibiotic or another marker which is an inheritable trait.

33. (new) A method according to claim 29, wherein RNA and protein expression levels are altered in the modified host cell as compared to the non-modified host cell.

34. (new) A method according to claim 29, wherein the modified host cell is a prokaryotic cell, a eukaryotic cell, a mammalian cell or a plant cell.

35. (new) A method for preparation of a modified host cell comprising:

- a) transfecting host cells with at least one DNA to which a fluorescent label is covalently coupled;
- b) separating transfected host cells, which contain the fluorescent label, from non-transfected host cells, which do not contain the fluorescent label, by detection of the fluorescent label;
- c) culturing the fluorescent label-containing host cells under proliferating conditions, whereby the fluorescent label is diluted and lost in progeny of the fluorescent label-containing host cells; and
- d) isolating a modified host cell from the cultured host cells, wherein a metabolic property of the modified host cell is permanently changed as compared to the non-transfected host cell.

36. (new) A method according to claim 35, wherein the modified host cell is not isolated by selection with an antibiotic or another marker which is an inheritable trait.

37. (new) A method according to claim 35, wherein RNA and protein expression levels are altered in the modified host cell as compared to the non-modified host cell.

38. (new) A method according to claim 35, wherein the modified host cell is a prokaryotic cell, a eukaryotic cell, a mammalian cell or a plant cell.